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(Cite as: 1990 WL 305551 (N.D.Cal.))

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United States District Court, N.D. California.
E.I. DU PONT DE NEMOURS & COMPANY, Plaintiff,
v.
CETUS CORPORATION, Defendant.
No. C-89-2860 MHP.

Dec. 3, 1990.

Clement L. Glynn, Pillsbury, Madison & Sutro, Walnut Creek, Cal., E. Anthony Figg, Bart G. Newland, Rothwell, Figg, Ernst & Kurz, Washington, D.C., George A. Frank, Senior Counsel, E.I. Du Pont de Nemours & Company, Wilmington, Del., for plaintiff.

Lynn Pasahow, James Lewis, McCutchen, Doyle, Brown & Enersen, San Francisco, Cal., for defendants.

ORDER

PATEL, District Judge.

*1 Plaintiff du Pont de Nemours & Company ("du Pont") brings this action against Cetus Corporation ("Cetus") for a declaratory judgment on the invalidity of two patents owned and controlled by Cetus. Cetus has brought a counter-claim for patent infringement. Du Pont is a Delaware corporation engaged in development, manufacture and distribution of pharmaceutical and diagnostic products; Cetus is a Delaware corporation engaged in development, manufacturing, sale and licensing of biotechnological products.

The parties are now before the court on plaintiff's motion for summary judgment on the invalidity of the disputed patents. Having considered the submissions and arguments of the parties, for the following reasons, the court DENIES plaintiff's motion for summary judgment.

Background

On July 28, 1987, the United States Patent and Trademark Office issued Patent No. 4,683,195 (" '195"), entitled "Process for Amplifying, Detecting and/or Cloning Nucleic Acid Sequence," and Patent No. 4,683,202 (" '202"), entitled "Process for Amplifying Nucleic Acid Sequences," to defendant Cetus Corporation. Both the '202 and '195 patents claim priority dating back to an application filed by Dr. Kary B. Mullis on March 28, 1985.

The two patents encompass the process of polymerase chain reaction ("PCR") using an exponential process of replication; the process permits a target sequence of DNA to be multiplied as quickly as a millionfold within hours. Kaster Decl. in Opp. to MSJ ("Kaster Decl."), Ex. I at 1543. The '202 patent describes the basic primer extension reaction, in which a target sequence of double-stranded DNA is denatured into single-stranded form by a process of heating. Two small pieces of synthetic DNA, each complementing a sequence at one end of the target sequence, serve as primers and bind with their complementary sequences on the single strand. Polymerases start at each primer, copying the sequence of that strand and ultimately producing exact replicas of the target sequence. The product of each cycle then serves as a template for succeeding cycles, resulting in an exponential process of replication. After repeated cycles, the pool of pieces of DNA with the target sequence has been greatly multiplied, and this amplified genetic material is available for further analysis. *Id.*

The disclosure of the '195 patent is similar to that of the '202 patent, with the additional disclosure of the use of a hybridization probe detection procedure in combination with PCR. This procedure requires adding to the product of the initial replication a labeled oligonucleotide probe for each segment being detected. The probe is a short segment of DNA capable of hybridizing to the segment and is labeled by incorporating radioactive atoms into its structure. The probe will bind to the target DNA through base pairing, so that the presence or absence of a particular sequence can be detected by determining whether the labeled probe has bound to the DNA of the substance being

analyzed. *Id.*, Ex. F at 4.

*2 The development of PCR has been widely recognized as "one of the most powerful tools of modern biology," and was honored with the "Molecule of the Year" award in *Science* magazine's summary of major scientific achievements of 1989. Def.Opp. to MSJ Ex. I. The rapid and relatively inexpensive amplification of specific DNA sequences can be used to diagnose disease, to detect trace amounts of pathogens that are difficult or impossible to culture, and to identify crime suspects, missing persons and suitable transplant donors through PCR-based comparisons. In addition, PCR may eventually replace gene cloning as the favored method of gene sequencing, a process which requires large amounts of DNA. Further applications of PCR are rapidly being discovered. *Id.* at 1543-44.

Plaintiff du Pont contends that PCR was in fact invented by scientists working in the laboratory of Dr. H. Gobind Khorana between 1969 and 1974, and that the subject matter of the '202 and '195 patents was anticipated by discussions of the technique and of Dr. Khorana's work in prior art published more than one year before the earliest filing date of the applications for '202 and '195. Du Pont argues that Cetus' patents are therefore invalid under 35 U.S.C. § 102 as anticipated by prior art, and invalid under 35 U.S.C. § 103 as obvious in the light of prior art.

Shortly after du Pont filed its declaratory judgment action on August 1, 1989, the United States Patent and Trademark Office ("PTO") ordered reexamination of all individual claims of the '202 patent pertinent to this motion [FN1] and of claims 19-25 of the '195 patent [FN2] pursuant to 35 U.S.C. §§ 301-307.[FN3] On March 19, 1990, the court granted Cetus' motion to delay trial until the reexamination had been conducted in order to permit the court to consider PTO's reexamination findings. Trial was set for November 27, 1990. Du Pont then filed its own requests for reexamination of '202 and '195, citing as prior art (among others) the articles by Kleppe et al. and Panet & Khorana that are also cited in defendant's brief. Kaster Decl., Ex. C at 4, Ex. D at 2. PTO consolidated the du Pont and Hoffman-LaRoche requests for joint consideration and decision. Kaster Decl., Exs. G & H. Plaintiff then brought this motion for summary judgment on August 16, 1990.

On August 23, 1990, PTO issued a decision upholding the validity of defendant's '202 and '195 patents in their entirety, specifically rejecting plaintiff's argument that PCR was anticipated by Kleppe et al. and Panet & Khorana. Kaster Decl., Exs. A & B.

LEGAL STANDARD

Under Rule 56 of the Federal Rules of Civil Procedure, summary judgment shall be granted "against a party who fails to make a showing sufficient to establish the existence of an element essential to that party's case, and on which that party will bear the burden of proof at trial ... since a complete failure of proof concerning an essential element of the nonmoving party's case necessarily renders all other facts immaterial." *Celotex Corp. v. Catrett*, 477 U.S. 317, 322 (1986). *See also T.W. Elec. Serv. v. Pacific Elec. Contractors Ass'n*, 809 F.2d 626, 630 (9th Cir.1987) (the nonmoving party may not rely on the pleadings but must present specific facts creating a genuine issue of material fact); *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 250 (1986) (a dispute about a material fact is genuine "if the evidence is such that a reasonable jury could return a verdict for the nonmoving party").

*3 The court's function, however, is not to make credibility determinations. *Anderson*, 477 U.S. at 250. The inferences to be drawn from the facts must be viewed in a light most favorable to the party opposing the motion. *T.W. Elec. Serv.*, 809 F.2d at 631.

Courts have held that summary judgment "is as appropriate in a patent case as in any other." *Barmag Barmer Maschinenfabrik AG v. Murata Mach., Ltd.*, 731 F.2d 831, 835 (Fed.Cir.1984). The nonmoving party "must point to an evidentiary conflict created on the record at least by a counter statement of a fact or facts set forth in detail in an affidavit by a knowledgeable affiant. Mere denials or conclusory statements are insufficient." *Id.* at 836.

DISCUSSION

The issues before the court are (1) whether claims 1-4, 6-9, 11, 16, 19 and 20 of the '202 patent are anticipated by the prior art cited by plaintiff ("Khorana prior art")

and are therefore invalid under 35 U.S.C. § 102(b); (2) whether those claims plus claim 15 of '202 define subject matter that would have been obvious to one of ordinary skill in March 1984 (one year prior to the filing date) in light of the Khorana prior art and the Khorana NSF Grant Proposal and are therefore invalid under 35 U.S.C. § 103; and (3) whether claims 1-4, 6, 11, 12, 14 and 15 of the '195 patent were obvious and well-known in March 1984 and therefore invalid under 35 U.S.C. § 103.

I. PRESUMPTION OF VALIDITY

With respect to suits involving the validity or infringement of a patent, the patent statute provides:

A patent shall be presumed valid. Each claim of a patent ... shall be presumed valid independently of the validity of other claims; dependent or multiple dependent claims shall be presumed valid even though dependent upon an invalid claim. The burden of establishing invalidity of a patent or any claim thereof shall rest on the party asserting such invalidity.

35 U.S.C. § 282. The courts have interpreted this presumption to require that the party asserting invalidity must prove facts establishing the invalidity of each claim by clear and convincing evidence. *Ethicon, Inc. v. Quigg*, 849 F.2d 1422, 1427 (Fed.Cir.1988) (citing *Kaufman Co. v. Lantech, Inc.*, 807 F.2d 970, 974 (Fed.Cir.1986)); *E.I. du Pont de Nemours & Co. v. Phillips Petroleum Co.*, 656 F.Supp. 1343, 1354 (D.Del.1987).

Moreover, although the court is not bound by the PTO's findings upholding the validity of the challenged patents in a reexamination proceeding, these findings affect the court's deliberations in two ways. First, they provide evidence that the court must consider in determining whether the plaintiff has overcome the statutory presumption of validity by clear and convincing evidence, *Fromson v. Advance Offset Plate, Inc.*, 755 F.2d 1549, 1555 (Fed.Cir.1985) (citing *American Hoist & Derrick Co. v. Sowa & Sons*, 725 F.2d 1350, 1359-60 (Fed.Cir.1984), *cert. denied*, 469 U.S. 821.

Secondly, where the patent has been reissued or upheld by the PTO, a challenger's burden of proving invalidity in subsequent litigation is heavier than it would otherwise be. *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1139 (Fed.Cir.1985) (citing *Fromson*, 755 F.2d at 1555); *see also Thermal Engineering Corp. v. Clean Air Systems*, 706 F.Supp. 436, 444 (W.D.N.C.1987) (successful **reexamination** of patent increases challenger's burden of proving invalidity). Specifically, courts have held that where a patent in suit has been reissued after the **PTO's** consideration of prior art cited by a challenger, the challenger's burden of proof in overcoming the presumption of validity in subsequent **litigation**"has become more difficult to sustain-a fact [ ] to be taken into account by the trial judge." *American Hoist*, 725 F.2d at 1364.

*4 The court therefore regards the **PTO's reexamination** findings of validity for all **claims** of '202 and '195 as highly probative on the issues considered and with respect to the prior art considered during **reexamination**. *See Fromson*, 755 F.2d at 1558; *American Hoist*, 725 F.2d at 1360. It thus views plaintiff's burden of proving invalidity as heavier than it would have been in the absence of the **reexamination**.

Although plaintiff properly notes that the **PTO proceedings** and the present suit challenging validity are independent, *see Ethicon*, 849 F.2d at 1428, and urges this court to reject the **PTO's** findings of validity of the challenged patents as flawed, the differences between the **PTO reexamination** and the present suit in fact suggest that the **PTO's** findings should be **given** substantial deference by this court.

First, whereas in **litigation** challenging validity the challenged patent enjoys a presumption of validity that the challenger must overcome by clear and convincing evidence, in a **reexamination proceeding**, the posture is essentially that of an initial **PTO** examination, and the patent enjoys no presumption of validity. *In re Etter*, 756 F.2d 852, 856-57 (Fed.Cir.), *cert. denied*, *Etter v. Commissioner of Patents and Trademarks*, 474 U.S. 828 (1985). It is therefore highly significant that the patents were upheld by the **PTO** against a higher standard than that to be applied by this court. In addition, the courts have recognized that one function of the **reexamination** finding is "to facilitate trial of that issue by providing the district

court with the expert view of the **PTO** (when a **claim** survives the **reexamination proceeding**)." *Ethicon*, 849 F.2d at 1426 (quoting *Gould v. Control Laser Corp.*, 705 F.2d 1340, 1342 (Fed.Cir.), *cert. denied*, 464 U.S. 935 (1983)).

Secondly, this **litigation** and the **PTO reexamination** differ in their approach to **claim construction** in a way which favors the patent owner in this **proceeding**. Whereas **claims** in **reexamination** "will be **given** their **broadest** reasonable interpretation," thus increasing the likelihood of a finding of anticipation and therefore of invalidity, *In re Etter*, 756 F.2d at 862 (quoting *In re Yamamoto*, 740 F.2d at 1571 (Fed.Cir.1984)), **claims** in **litigation** are to be "so construed, if **possible**, as to sustain their validity." *Id.* (quoting *ACS Hospital Systems, Inc. v. Montefiore Hospital*, 732 F.2d 1572, 1577 (Fed.Cir.1984)).

Finally, plaintiff du Pont was one of the parties requesting **reexamination** and made essentially the same arguments (citing essentially the same references) before the **PTO** as it makes before the court today. In a **reexamination proceeding**, the Examiner may consider any information or prior art **not** considered at the time of the initial examination. 35 U.S.C. § 301 et seq.; *In re Etter*, 756 F.2d at 856. Plaintiff's requests for **reexamination** of '202 and '195 alleged that the patents were anticipated by or obvious in light of Kleppe et al. and Panet & Khorana, among other references, and were supported by declarations of Dr. Joseph Sambrook and Dr. Arthur Kornberg; these references and declarations are also heavily relied upon by plaintiff in this suit. The Examiner made specific findings rejecting the claims of anticipation by Kleppe et al, Kaster Decl.Ex. B at 4, and Panet & Khorana, Kaster Decl.Ex. A at 8, Ex. B at 8.

***5** This court will follow the approach of the Federal Circuit in giving deference to PTO findings with respect to the evidence considered by PTO. *American Hoist*, 725 F.2d at 1360. "When an attacker simply goes over the same ground travelled by the PTO, part of the *burden* is to show that the PTO was wrong in its decision to grant the patent." *Id.*[FN4]

However, plaintiff also alleges anticipation of '202 by a National Science Foundation grant proposal submitted by Dr. Khorana in 1972 ("Khorana Grant Proposal"). Pl.MSJ Ex. E, a reference not cited in plaintiff's request for reexamination and not considered by the Examiner. The courts have held that the deference due to PTO findings upon reexamination is appropriate only with respect to the evidence and prior art that was before both the PTO examiners and the court.

Deference is due the Patent and Trademark Office decision to issue the patent with respect to evidence bearing on validity which it considered but no such deference is due with respect to evidence it did not consider. All evidence bearing on the validity issue, whether considered by the PTO or not, is to be taken into account by the tribunal in which validity is attacked.

American Hoist, 725 F.2d at 1360; *see also In re Etter*, 756 F.2d at 861 (Nies, J., concurring). The court will therefore consider directly the question of anticipation by the Khorana Grant Proposal.

Finally, although PTO directly ruled that '202 and '195 were valid because they were not anticipated by prior art pursuant to 35 U.S.C. § 102, it did not address the question of whether the patents were invalid under the obviousness standard of 35 U.S.C. § 103. The court will therefore consider this question independently. *See In re Etter*, 756 F.2d at 856 (reexamination is available under 35 U.S.C. §§ 102 and 103).

II. ANTICIPATION OF '202 BY KHORANA PRIOR ART UNDER 35 U.S.C. § 102

The statute governing patentability provides that:

[a] person shall be entitled to a patent unless- ...

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States, ...

35 U.S.C. § 102(b).

Anticipation requires that each prior art reference contain within its four corners all of the elements of

the claimed invention found in substantially the same situation where they do substantially the same work in the same way. *Atlas Powder Co. v. E.I. du Pont de Nemours and Co.*, 588 F.Supp. 1455 (D.C.Texas 1983), *aff'd*, 750 F.2d 1569; *Ecolochem, Inc. v. Mobile Water Technology Co.*, 690 F.Supp. 778 (E.D.Ark.1988), *aff'd*, 871 F.2d 1096 (Fed.Cir.1989). Prior art does not anticipate a thing or process unless it is enabling: an anticipatory publication must describe the claimed invention with sufficient clarity and specificity so that one skilled in the relevant art could practice the subject matter of the patent without assistance from the patent claimed to have been anticipated. *Columbia Broadcasting System v. Sylvania Elec. Products, Inc.*, 415 F.2d 719, 725, (1st Cir.1968), *cert. denied*, 396 U.S. 1061 (1970). "[B]efore any publication can amount to a statutory bar to the grant of a patent, its disclosure must be such that a skilled artisan could take its teachings in *combination with his own knowledge of the particular art and be in possession of the invention.*" *Titanium Metals Corp. v. Mossinghoff*, 603 F.Supp. 87, 90 (quoting *In Application of LeGrice*, 301 F.2d 929 (C.C.P.A.1962)) (D.C.C.1984) (emphasis in original).

*6 Plaintiff asserts that PCR was anticipated by (1) K. Kleppe, et al., "Studies on Polynucleotides: Repair Replication of Short Synthetic DNA's as catalyzed by DNA Polymerases," published in the *Journal of Molecular Biology* in 1971 ("Kleppe et al."); (2) A. Panet and G. Khorana, "Studies on Polynucleotides: the Linkage of Deoxyribopolynucleotide Templates to Cellulose and its Use in Their Replication," published in the *Journal of Biological Chemistry* in 1974 ("Panet & Khorana"); and (3) Dr. Khorana's National Science Foundation ("NSF") Grant Proposal, submitted in 1972 ("Khorana Grant Proposal"). Plaintiff contends that claims 1-4, 6-9, 11, 16, 19 and 20 of '202 are therefore invalid under 35 U.S.C. § 102.[FN5]

In support of its claim that each of the cited references anticipates PCR, plaintiff relies upon a claim-by-claim comparison of the patent claims with the cited references and upon the testimony of Dr. Kornberg that the references would have enabled a skilled biochemist to practice PCR but for the fact that the primers necessary for the process were scarce and extremely difficult to chemically synthesize until March 1984. Kaster Decl., Ex. E ¶¶ 14-19.

PTO's findings and the declarations of scientists submitted by Cetus concluded that the publications by Kleppe et al. and Panet & Khorana are too indefinite and uncertain to anticipate PCR, in part because they fail to specify the precise nature of the primers to be used, the size of DNA duplex to be copied, or specific reaction conditions required for DNA synthesis,[FN6] and that the Khorana grant proposal similarly does not anticipate PCR. The court finds that the PTO rulings and the evidence presented on this motion present genuine issues of material fact, making plaintiff's motion for summary judgment inappropriate.

A. *PTO Re-examination*

The PTO Examiner specifically upheld the validity of all challenged claims of '202 and '195, finding that they were not anticipated by Kleppe et al. and Panet & Khorana. Kaster Decl., Ex. A at 3-8; Ex. B at 2-8. The Examiner found unpersuasive the assertions of the Kornberg and Sambrook declarations that Panet & Khorana teaches PCR. Kaster Decl., Exs. A & B.

In challenging the **PTO** findings, plaintiff argues that the Examiner committed numerous errors in affirming the patentability of '202 and '195 as against the prior art cited by plaintiff. The court finds most of these allegations to be without merit.

1. ***PTO** Procedure.* Plaintiff protests that it was **not** permitted "further input" into the **proceedings** beyond its initial **reexamination** request and was prejudiced by that exclusion. However, a **reexamination** by the **PTO** is **not** an adversary **proceeding** of the sort that occurs in **litigation**; although a third party may bring a request for **reexamination**, that party is heard only on the question of whether "a substantial question" of validity exists justifying the **reexamination** procedure. "[T]he **reexamination***per se* of the **claims** is entirely *ex parte*." *In re Etter*, 756 F.2d at 859 n. 6; *see also*37 C.F.R. § 1.550(e) ("The active participation of the **reexamination** requester ends with the reply pursuant to § 1.535, and no further submissions on behalf of the **reexamination** requester will be acknowledged or considered.").

*7 Moreover, the Examiner expressly considered and

rejected plaintiff's assertions of anticipation by Kleppe et al. and Panet & Khorana, and specifically discussed the opinions expressed in the Sambrook and Kornberg declarations.

Plaintiff also faults Cetus for failing to inform the Examiner of material in statements, deposition testimony and deposition exhibits that, in plaintiff's judgment, tended to show that the Khorana prior art anticipated '202 and '195. However, the statute governing reexamination, 35 U.S.C. § 301 et seq., nowhere imposes upon the patent owner a duty to identify and disclose to the Examiner all evidence that might arguably invalidate the patent under reexamination; nor does plaintiff cite any case law indicating that courts have imposed such a duty. Indeed, it is precisely the duty of *the requester* to cite prior art alleged to have a bearing on the patentability of a challenged **claim**. 35 U.S.C. §§ 301-302.

2. ***PTO** Findings.* Du Pont alleges that the Examiner misapplied the law in its **reexamination** of '202 and '195 by **requiring** a degree of specificity in the prior art **not** present in the patents being challenged.

The statute governing **reexamination** provides that a patent owner may appeal an adverse **reexamination** finding to the United States Court of Appeals for the Federal Circuit. 35 U.S.C. § 306. However, this court has no power to review a **PTO** finding favorable to the patent owner at the behest of a patent challenger such as du Pont. *See Syntex (U.S.A.) Inc. v. United States PTO*, 882 F.2d 1570, 1573 (Fed.Cir.1989); *accord Yuasa Battery Co. v. Commissioner of Patents & Trademarks*, 3 U.S.P.Q.2d 1143, 1144 (D.D.C.1987).

Although plaintiff is **not** here requesting that the court exceed its jurisdiction and set aside the **reexamination** decision, it is requesting this court to find that the **PTO** was wrong in its decision to grant the patent, and to refuse to accord the **PTO** rulings the deference prescribed by the Federal Circuit. Courts have asserted jurisdiction to invalidate a reissued patent (an amended patent reflecting corrections of error in an original patent) that is "found to be procured as a result of fraud or inequitable conduct, or when the patent was issued despite a failure to satisfy the statutory requirements, such as non-obviousness." *Hewlett-Packard Co. v. Bausch & Lomb, Inc.*, 692 F.Supp. 1118, 1123 (N.D.Cal.1988), *aff'd in part, rev'd on other grounds in part*, 882 F.2d 1556 (Fed.Cir.1989), *cert. denied*, --- U.S. ----, 110 S.Ct. 1125 (1990).

The court finds that the PTO reexaminations of '202 and '195 appropriately considered and applied the statutory requirements for anticipation to Kleppe et al. and Panet & Khorana. The Examiner found a substantial lack of detail and uncertainty about the formation of template-primer complexes in Kleppe et al., Kaster Decl., Ex. A at 3-4, Ex. B at 3-4, and critical ambiguities in the disclosure of Panet & Khorana, *Id.*, Ex. A at 4-8, Ex. B at 4-8, sufficient to preclude anticipation of the two patents. The Examiner also rejected du Pont's explanation that PCR had not been performed prior to 1984 because of the scarcity of oligonucleotide primers. *Id.*, Ex. A at 7-8. Finally, the Examiner found that Panet & Khorana did not disclose the use of exponential replication, as expressly required by claims 1 and 19 of the '202 patent, *Id.*, Ex. A at 8, Ex. B at 2, and Claim 19 of the '195 patent. *Id.*, Ex. A at 2-3.

*8 This court thus finds persuasive the PTO's conclusion that Kleppe et al. and Panet & Khorana do not anticipate PCR.

B. *Expert Testimony*

Moreover, the court finds that the Coggio, Dahlberg and Smith Declarations and attached exhibits provide additional strong support for the conclusion that Kleppe et al., Panet & Khorana, and the Khorana grant proposal [FN7] do not anticipate PCR. These sources conclude that the experimental conditions, parameters, concentrations, and techniques discussed in the references are both quantitatively and qualitatively different from those of the patented process of '202. Kaster Decl.Ex. A at 3-4, Ex. B at 4-8; Coggio Decl., Ex. A at ¶¶ 7-10, 13; Dahlberg Decl. at ¶¶ 14-18, 28; Smith Decl. at ¶¶ 6-17. At a minimum, these sources raise a substantial issue of material fact making summary judgment inappropriate. "[A] patent case is not ripe for summary judgment on the issues of validity or enforceability ... where the expert testimony submitted is conflicting...." *Acoustiflex Corp. v. Owens-Corning Fiberglass Corp.*, 572 F.Supp. 936, 937 (N.D.Ill.1983).

The court therefore finds that plaintiff has failed to demonstrate that no material issues of fact remain in dispute as to the invalidity of '202 under 35 U.S.C. § 102(b).

III. OBVIOUSNESS OF '202 AND '195 UNDER 35 U.S.C. § 103

In addition to arguing that '202 is anticipated by prior art, plaintiff argues that claim 15 of '202, even if not technically anticipated by the cited references, and claims 1-4, 6, 11, 12, 14 and 15 of '195 are invalid under 35 U.S.C. § 103, which provides that an invention is not patentable if

the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains....

Although the ultimate question of patent validity is a question of law, the inquiry into obviousness under § 103 has been held to require factual findings on the following issues: (1) the scope and content of the prior art; (2) differences between the prior art and the claims at issue; and (3) the level of ordinary skill in the pertinent art. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966); *Custom Accessories v. Jeffrey-Allan Indus.*, 807 F.2d 955, 958 (Fed.Cir.1986). In addition, secondary considerations such as commercial success, long-felt but unsolved needs, failure of others to perform the claimed invention, and copying of the invention in preference to prior art are relevant as indicia of obviousness or non-obviousness. *Graham*, 383 U.S. at 17-18; *Spalding & Evenflo Companies, Inc. v. Acushnet Co.*, 718 F.Supp. 1023, 1044 (D.Mass.1989).

A claim of obviousness under section 103 challenges the inventiveness of the patent and is required to meet a less stringent standard than a claim of anticipation under section 102, which challenges the novelty of the patent. *Shanklin Corp. v. Springfield Photo Mount Co.*, 521 F.2d 609, 617 (1st Cir.1975), *cert. denied*, 424 U.S. 914 (1976); *Hart v. Baarcke*, 396 F.Supp. 408, 412 (S.D.Fla.1975), *aff'd*, 550 F.2d 353 (5th Cir.1977). Obviousness can be shown by appeal to (1) any combination of prior art references (no one of which need disclose all elements of the invention within its four corners); (2) obviousness to one of ordinary skill in the pertinent art; and (3) secondary considerations such as commercial success of the invention.

A. *'202 Patent*

*9 Plaintiff alleges that Claim 15 of '202, requiring that the primers must be present "in a molar ratio of at least 1000:1 primer:complementary strand," is obvious under section 103. Plaintiff cites the reference in Kleppe et al. to the use of a "sufficiently large excess of the two appropriate primers"; the specification in Panet & Khorana that a large excess (ten times or more) of the primer be used; and the specification in the Khorana Grant Proposal that an excess of primers was needed. Plaintiff argues that these assertions in the prior art, in conjunction with the sharp increase in availability of primers in the 1980s and the then-available knowledge concerning hybridization kinetics, made a ratio of 1000:1 "an obvious choice."

In the court's judgment, references to a ratio of "ten times or more" and general references to a "sufficiently large excess" do not make the use of a primer:strand ratio of 1000:1 necessarily "obvious." This contention is put in issue by defendant's experts, who discuss the inadequacies of the prior references in great detail and conclude that they were inoperable. *See, e.g.*, Smith Decl. at ¶¶ 15-18.

The court concludes that plaintiff has failed to carry its burden of showing that there is no genuine issue of material fact on the invalidity of Claim 15 of '202 under 35 U.S.C. § 103.

B. *'195 Patent*

The '195 patent discloses the combination of hybridization probe detection with PCR. Plaintiff argues that since the PCR process described by Claim 1 of '202 was either anticipated or obvious in March of 1984 (thus invalidating '202) and the probe detection procedure with DNA cloning was well-known by that time, it would have been obvious to combine the two, thus rendering claims 1-4, 6, 11, 12, 14 and 15 of '195

invalid under section 103. Because the court has concluded that there is sufficient dispute over material issues of fact to deny summary judgment on the obviousness of '202, it cannot accept the first premise of this argument.

Moreover, plaintiff's reliance on the testimony of Dr. Kary Mullis, the named inventor of the '202 patent and named co-inventor of the '195 patent, as to the obviousness of using PCR with the probe detection procedure is inapposite. As defendant notes, the inquiry into obviousness focuses on what would have been obvious to "a *hypothetical* 'person having ordinary skill in the art.' The actual inventor's skill is irrelevant to the inquiry.... [O]ne should not go about determining obviousness under § 103 by inquiring into what *patentees* (i.e., inventors) would have known or would likely have done...." *Standard Oil Co. v. American Cyanimid Co.*, 774 F.2d 448, 454 (Fed.Cir.1985) (emphasis in original).

Plaintiff argues that by 1984, the procedure of hybridized probe detection disclosed in '195 was already a well-known method of detecting and identifying specific sequences of DNA and had been described in the technical literature, including *Molecular Cloning-A Laboratory Manual* (published in 1982). Specifically, the *Cloning Manual* refers to the use of DNA cloning to enhance hybridization probe detection. Sambrook Decl. (Newland Decl.Ex. D) at ¶ 12; *id.* at Attachment 2. Defendant does not dispute that the technique was well-known and widely used by March 1984, but argues that its use in combination with PCR was not obvious under section 103 because PCR itself was not obvious under section 103.

***10** Having found that the claims of '202 are not obvious under section 103, the court concludes that the combination of PCR with hybridization probe detection, disclosed by '195, is likewise not obvious.

C. *Secondary Considerations*

The inquiry under section 103 may include such secondary considerations as commercial success of the patent, long-felt but previously unsolved needs, and failure of others to perform the invention as evidence of obviousness or non-obviousness, *Graham*, 383 U.S. 1 (1966), although such considerations are not by themselves sufficient to establish non-obviousness. *Eltra Corp. v. Basic, Inc.*, 599 F.2d 745 (6th Cir.), *cert. denied*, 444 U.S. 942 (1979).

In this case, secondary considerations support a finding of nonobviousness of the claims in '202 and '195. At best, defendant's submissions show that there are clear disputes among qualified experts. The commercial success and expanding potential of the process are clear. Smith Decl., Ex. D; Kaster Decl., Ex. I at 1543-44; Kaster Decl., Ex. K. Defendant has also provided evidence of the long-felt need in the field and of the failure of others to perform PCR prior to the work of Dr. Mullis at Cetus. Dahlberg Decl. ¶¶ 23-26; Smith Decl. ¶¶ 16-17; Klug Decl. (Coggio Decl., Ex. A) at ¶¶ 13-16; White Decl. (Coggio Decl., Ex. B) at ¶¶ 10-13.

Because the court concludes that the plaintiff has failed to meet its burden of proving that there is no genuine issue of material fact on the anticipation or obviousness of '202, and plaintiff's proffer of the testimony of Dr. Mullis does not satisfy the requirements of a showing under section 103, the court finds that the plaintiff also has failed to meet its burden on the obviousness of '195.

CONCLUSION

The findings of PTO and the declarations of the experts submitted by defendant raise genuine issues of fact on the questions of anticipation of '202 by prior art under 35 U.S.C. § 102 and the obviousness of '202 and '195 under 35 U.S.C. § 103. The court concludes that plaintiff has not demonstrated by clear and convincing evidence that no genuine issues of fact remain. Plaintiff's motion for summary judgment in its suit for declaratory judgment on the invalidity of '202 and '195 is therefore DENIED.

IT IS SO ORDERED.

FN1. Du Pont challenges **claims** 1-4, 6-9, 11, 15, 16, 19 and 20 of the '202 patent.

FN2. Du Pont also challenges the validity of **claims** 1-4, 6, 11, 12, 14 and 15 of the '195 patent as invalid under 35 U.S.C. § 103. **PTO**

found no new question of patentability with respect to **claims** 1-18 and 26, and declined to **reexamine** those **claims**.

FN3. This **reexamination** was ordered at the request of Hoffman-LaRoche, Inc., one of Cetus' principal PCR licensees.

FN4. Although the court finds that the **reexamination** rulings are to be accorded the deference prescribed by the Federal Circuit and other courts, du Pont would still bear the burden of proof on invalidity by clear and convincing evidence if the court found the **reexamination** rulings defective either procedurally or on the merits. **Reexaminations** which affirm the validity of a challenged patent increase the challenger's burden in **litigation**, but a court's decision **not** to defer to the Examiner's ruling does **not** decrease the challenger's burden. "[T]he burden of persuasion on the merits remains with [the party asserting invalidity] until final decision.... With all evidence in, *the trial court* must determine whether the party on which the statute imposes the burden of persuasion has carried that burden." *In re Etter*, 756 F.2d at 856 (quoting *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1534 (Fed.Cir.1983)).

FN5. In addition, plaintiff asserts that claim 15 of '202 is invalid under section 103 because it defines subject matter that would have been obvious to one of ordinary skill in March 1984 in view of the prior art cited by plaintiff. *See below* at section III.

FN6. At oral argument, plaintiff urged that the '202 patent suffers the same deficiencies of indefiniteness and uncertainty. Pointing to claim 1, plaintiff contends that the claim provides no greater specificity than does the prior art. Plaintiff appears to be arguing that the patent is non-enabling. However, the dependent claims of '202 provide the specificity and limitations plaintiff finds missing. For example, dependent claims 14-17 contain some of the details missing from the prior art.

FN7. Plaintiff cites as prior art the Khorana NSF grant proposal, a reference not cited in du Pont's request for reexamination before the PTO. As a preliminary matter, plaintiff asserts that the proposal was a publicly accessible document prior to March 1984 and therefore qualifies as a "printed publication" under 35 U.S.C. § 102(b). Defendant contends that the grant proposal was not a printed publication because, although available to the public upon request from NSF, it was not subject-matter indexed and had a vague title ("Chemical and Biological Studies of Nucleic Acids") that would not have disclosed its relevance to one interested in PCR-related technology. However, plaintiff points out that the Khorana Grant Proposal was indexed by title, author, institution and grant number; has been available upon request from NSF under the Freedom of Information Act; and was cited by grant number on the first page of Panet & Khorana. Newland Decl., Ex. G at 5213. Any researcher interested in DNA replication is likely to have been familiar with Panet & Khorana and therefore would have been alerted to the relevance of the Khorana Grant Proposal both from the reference to the Grant Proposal and from the identity of its author, who was widely recognized as a pioneer in the field of DNA synthesis. The court thus agrees with plaintiff that "[t]he title [of the Grant Proposal], taken in combination with Dr. Khorana's reputation, would lead anyone interested in DNA synthesis or replication to believe that the reference was pertinent to such technology." Pl.Rep. MSJ at 7-8. *See also In re Hall*, 781 F.2d 897, 899-900 (Fed.Cir.1986) (doctoral thesis indexed, catalogued and shelved at university library was "printed publication" under section 102(b)).

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